## **Imaging on Structural Lateralization**

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<u>Abstract</u> Owing to various acquisition schemes, it is challenging and time-consuming to compare the quantitative indices derived from different MR methods. In this study, we used diffusion spectrum imaging (DSI) to analyze structural lateralization of arcuate fasciculus and a sub-sampling approach was performed to correlate with diffusion tensor imaging (DTI). Our results showed that both diffusion indices and lateralization indices are highly correlated between DTI and DSI, which suggests that the structural analysis among diffusion MR methods is comparable. This study might be the first one that compares diffusion indices and lateralization between different diffusion methods in neuroscience study, which may facilitate inter-sites collaborations of diffusion MR researches.

Introduction Since 1970s, the hemispheric lateralization has been investigated in various fields of neuroscience [1-3]. Recently, using advanced imaging modalities, such as PET and MRI, to study hemispheric lateralization has been reported [4-7]. By combining functional MRI (fMRI) and diffusion tensor imaging (DTI), Vernooij et al. reported the structural asymmetry of arcuate fasciculus and its association with functional language lateralization by considering hand preference and sex [9]. Beyond DTI, diffusion methods to resolve multiple crossing-fibers, such as diffusion spectrum imaging (DSI) and q-ball imaging (QBI) were considered much more accurate in depicting complex fiber architecture and quantifying the diffusion characteristics. In this study, we aimed to use DSI to study the structural lateralization and a tract-specific analysis was performed with anisotropic index along the arcuate fasciculus (AF), which is essential to language networks. In addition, DTI was reconstructed using a subset of DSI data and same tract-specific analysis was performed to investigate the correlation between DSI and DTI anisotropic indices.

Materials and Methods Twenty normal Chinese volunteers, 10 right-handers and 10 left-handers classified by the Edinburgh Handedness Inventory, were studied.

DSI data were acquired with a 3T MRI system (Trio, Siemens, Erlangen, Germany) using twice-refocused balanced echo diffusion EPI sequence. A total of 203 diffusion-encoding gradients with maximum b-value =  $6000 \text{ s/mm}^2$  were sampled on the grid points with the radius  $|\mathbf{q}| \le 3.6$  units over the 3D q-space. The imaging parameters were TR/TE = 9100/142 ms, an isotropic resolution of  $2.9^3 \text{ mm}^3$  and slice numbers = 45. DSI analysis was based on the relationship that the echo signal S( $\mathbf{q}$ ) and the diffusion probability density function P( $\mathbf{r}$ ) were a Fourier pair, i.e., S( $\mathbf{q}$ ) = FT{P( $\mathbf{r}$ )} [10]. The orientation distribution function (ODF) was determined by computing the second moment of P( $\mathbf{r}$ ) along each radial direction. The main orientation of diffusion probability was then determined by the local maximum vectors of ODF [11-12]. Generalized fractional anisotropy (GFA) index was derived from DSI ODF followed by Tuch's definition [13].

To investigate the structural lateralization using DTI index, we estimated a subset of DSI data which was most appropriate for reconstructing the diffusion tensor. According to the proportionality between  $|q|^2$  and the b-value, the b-value at any grid point  $(q_x, q_y, q_z)$  in the q-space can be computed by  $6000 \times (q_x^2+q_y^2+q_z^2)/3.6^2$ . To obtain the optimum DTI data in our case, the relationship between signal-to-noise ratio (SNR) and the number of sub-sampled diffusion data set was investigated. The SNR was defined as  $(N)^{1/2} \times e^{-bavgD}$ , where N is the number of sub-sampled data set, bavg is the averaged b-value of the sub-sampled data set and D is the diffusion coefficient, approximately  $5 \times 10^4$  mm<sup>2</sup>/s [14]. The sub-sampled data set that yielded the highest SNR was considered the optimum data set for DTI reconstruction. Based on our DSI data, we found that the optimum data set for DTI was N = 81, corresponding to the grid points in the q-space with radii less than 2.45 units, and bavg of 2770 s/mm<sup>2</sup>. DTI was then reconstructed based on the standard procedures and fractional anisotropy (FA) index was derived voxel-by-voxel [15].

In this study, a tract-specific analysis was performed along AF, which was reconstructed from DSI data. We used MARINA (Bender Institute of Neuroimaging, University of Giessen, Germany) to choose opercular and triangular parts of inferior frontal gyrus on MNI coordinate as seeding area, and transformed it to the  $B_0$  images of individual participants using the normalization information generated by SPM5. A streamline-based tracking algorithm was then applied to the seeding area and the tracts generated from this area and marched toward temporal lobe were selected as AF. DSI GFA values along right and left AF were averaged separately to estimate the diffusion characteristics. Similarly, the averaged FA values of both right and left AF were calculated. Lateralization index (LI) was calculated from these two indices, i.e. DSI GFA and DTI FA, and defined as LI = (L-R)/(L+R), where L and R indicated the averaged values of GFA or FA on left and right AF respectively.

<u>**Results</u>** The scatter plots of DSI GFA *vs.* DTI FA were shown in Fig (a-c), which shows significant positive correlation between these two indices in all of the three groups, i.e. right-handed (R = 0.9211), left-handed (R = 0.6198) and all volunteers (R = 0.9088). This indicates that there was a high correspondence between DSI GFA and DTI FA and the reliability of these two indices was demonstrated. As shown in Fig (d-f), the scatter plots of LI derived from DSI GFA and DTI FA also show significantly positive correlation. Fig (d) shows that positive structural lateralization was found in right-handed group using either DSI GFA or DTI FA. However, no significant structural lateralization was found in left-handed group as shown in Fig (e).</u>

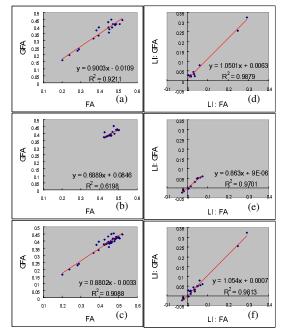


Fig (a-f). Correlation plot of results from DTI and DSI. The first column indicates correlation between FA and GFA, and the second one indicates correlation between lateralization calculated by FA and GFA. The first row indicates correlation for right-hander group (a and d), the second one indicates correlation for left-hander group (b and e), and the third one for the all the 20 volunteers (c and f).

**<u>Reference</u>** [1] Galaburda et al., 1978. [2] Rubinao, 1970. [3] Schwartz et al., 1975. [4] Bookheimer et al., 1997. [5] Binder et al., 1995. [6] Desmond et al., 1995. [7] Price, 2000. [8] Vernooij, 2007. [9] Hagmann et al., 2006. [10] Callaghan, 1991. [11] Wedeen et al., 2005. [12] Lin et al., 2003. [13] Tuch, 2004. [14] Wu et al., 2007. [15] Basser, 1995.

**Discussion** In this study, the significantly positive correlation between DSI GFA and DTI FA shows the reliability of these two anisotropy indices. The structural lateralization was revealed in right-handed group, which suggests that both DSI GFA and DTI FA can provide potentially promising quantification of diffusion characteristics. In our results, there was no significant structural lateralization in the left-handed group, which may be a combining effect of handedness and sex. Therefore, the structural lateralization power and comparison between DSI and optimized DTI have to be investigated with further experiment design.